UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/752,453 | 01/03/2001 | Samario Chaitchik | 381/25 | 2182 |

7590 03/28/2002

DR. MARK FRIEDMAN, LTD.
C/O BILL POLKINGHORN- DISCOVERY DISPATCH
9003 FLORIN WAY
UPPER MARLBORO, MD 20772

| EXAMINER |
|---|
| GABEL, GAILENE |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | 6 |

DATE MAILED: 03/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/752,453 | Applicant(s) CHAITCHIK ET AL. | |
|---|---|---|---|
| | Examiner Gailene R. Gabel | Art Unit 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Claims Under Examination*

1. Claims 1-13 are pending and under examination.

### *Drawings*

2. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached).

### INFORMATION ON HOW TO EFFECT DRAWING CHANGES

**A. Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

**B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

**C. Timing of Corrections**

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step b) is ambiguous in reciting, "exposing a portion of the cells to a drug" because the term "a portion" is a relative term that lacks a comparative basis for defining its metes and bounds. Specifically, how is the portion of cells selectively exposed to a portion of the cells. See also step e).

Claim 1, step c) is indefinite in reciting "capable of" and "can be" because it fails to recite a positive limitation in the claim.

Claim 1, step c) is indefinite in reciting, "substance ... imparting a measurable degree of fluorescence" because it implies but fails to specifically define that the substance is a fluorescent substance.

Claim 1 step d) is ambiguous in reciting, "causing the cells to reside" because it does not specifically define how cells are "caused to reside ... in defined locations".

Claim 1, step d) is indefinite in reciting "can be" because it fails to recite a positive limitation in the claim.

Claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. A correlation step correlating the "assay result" to drug sensitivity of the cells is missing.

Claim 8 is indefinite in reciting "capable of" because it fails to recite a positive limitation in the claim.

Claim 8 is indefinite in reciting, "substance ... imparting a measurable degree of fluorescence" because it implies but fails to specifically define that the substance is a fluorescent substance.

Claim 9 is indefinite in reciting, "capable of" because it fails to recite a positive limitation in the claim.

Claim 9 is indefinite in reciting, "substance ... imparting a measurable degree of fluorescence" because it implies but fails to specifically define that the substance is a fluorescent substance.

Claim 9 is indefinite in reciting, "overlapping Markush groups."

Claim 10 is indefinite in reciting, " further including the step of" because it is unclear what other steps are further included in the claim.

Claim 11 is indefinite in reciting, " further including the step of" because it is unclear what other steps are further included in the claim.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4 and 7-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,180,343) in view of (Weinreb et al. (US 4,729,949).

Anderson et al. disclose a method of testing sensitivity of cells to drugs comprising candidate nucleic acids. Anderson et al. teach preparing a suspension of cells then exposing the cells to the nucleic acids. Nucleic acids are encapsulated with liposome then introduced into the cells by liposome fusion. The cells are incubated and cultured to optimize growth and proliferation of the cells then are timely harvested. See column 19, line 38 bridging to column 20, line 3. Exogenous nucleic acids are also introduced by viral infection (see column 20, lines 45-54). The drug sensitivity method allows selection of cells that exhibit sensitivity by virtue of altered phenotype as a consequence of the presence of the peptide within the cell (see column 20, line 64 to column 21, line 16). Anderson et al. also teach labeling the nucleic acid with GFP or fluorescent dyes to impart a measurable degree of fluorescence (see column 22, lines 32-41). Cells exhibiting an altered phenotype or change in physiology is due to the sensitivity of the cells to the nucleic acid as a bioactive peptide. These phenotypic alterations or pharmacologic effects are manifested depending on the sensitivity of cells to the nucleic acid (see columns 23-24 and 35). Accordingly, sensitivity of cells to the nucleic acid is detected and measured by microscopic analysis of cellular morphology, standard assay for the presence of a particular cell or molecule manifested by the phenotypic alteration, and flow activated cell sorting (FACS) (see column 23, lines 54-

67). Anderson et al. teach detecting and measuring GFP using scanning densitometer, BioImage software, and BD FACSCAN and calculating specific fluorescence, i.e. ratio of the average fluorescence to the relative intensity and standard deviation of fluorescence intensity (see column 38).

Anderson et al. differ in failing to disclose causing the cells to reside individually in defined locations wherein each individual cell corresponds to the defined location and accessed individually by an assay device for assaying and determining the sensitivity of the drug.

Weinreb et al. disclose a method for placing individual living cells at defined locations wherein a fluid containing living cells is applied to a carrier having a plurality of apertures arranged in an ordered array and sized specifically to hold individual cells. The cells are cause to migrate into the apertures to the defined locations by applying a force or pressure differential (see Abstract and column 8, line 58 to column 9, line 13). Excessive and other cells are washed off at least once. The fluorescence of each cell on the defined locations in the carrier is separately measured and recorded. Examples of measurable and calculable parameters include fluorescence intensity, degree of fluorescence polarization, light scatter, optical density, electromagnetic properties, and information or data obtained is processed, recorded, plotted, and stored in a computer system. Standard errors are obtained by comparison to control values for recordation to eliminate outliers from values within a standard deviation (see columns 16-18 and 23-24).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have harvested the cells in the method of Anderson for drug sensitivity assaying using the cell carrier system taught by Weinreb because Weinreb specifically taught that the carrier provides better separation of cells that have been selected for assaying; thus enabling better determination and accuracy in testing for drug sensitivity of cells selected.

4. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 6,180,343) in view of (Weinreb et al. (US 4,729,949) as applied to claims 1-4 and 7-13 above, and further in view of Condon et al. (US 6,168,944).

Anderson et al. and Weinreb et al. have been discussed supra. Anderson et al. and Weinreb et al. differ in failing to disclose harvesting the cells using trypsin.

Condon et al. teach large scale cultivation cells wherein trypsin is used to dissociate and harvest cells from microcarriers in bioreactors.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have harvested the cells in the method of Anderson as modified by Weinreb using trypsin to dissociate the cells from microcarriers because Condon specifically taught that trypsin is a known proteolytic enzyme for use in dissociating and harvesting cells in large scale cultivation of cells such as in the methods disclosed by Anderson and Weinreb.

5. No claims are allowed.

***Remarks***

6. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Keusch et al. (US 5,955,293) disclose assays for shiga toxin and shiga-like toxins.

Yokoyama (US 6,046,044) discloses methods for identifying cisplatin resistance tumor cells using nucleic acids and proteins of the invention.

Watson et al. (US 5,998,159) disclose methods for screening for test compounds such as antibiotics.

Sarkadi et al. (US 5,872,014) disclose assay and diagnosis of multi-drug resistance in patients.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
March 21, 2002

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
03/24/02